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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/650,559	08/28/2003	Jeffrey A. Engler	P66186US01GP	1600

23378 7590 02/03/2009

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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
02/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/650,559	ENGLER ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/28/2003, 2/6/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment, filed on 11/19/2008 is acknowledged. Claims 36-48 are cancelled. Claims 49-55 are amended.

Election/Restrictions

Applicant's election without traverse of Group II in the reply filed on 11/19/2008 is acknowledged.

Claims 49-55 are pending and are currently under examination.

Information Disclosure Statement

The information disclosure statements filed on 8/28/2003 and 2/6/2004 are acknowledged. Initialed copies are enclosed.

Specification

This application fails to comply with the requirements of 37 C.F.R. 1.821-1.825 because it contains amino acid sequences that are not identified. For example, Figure 3 contains sequences that are not identified. Each sequence in the drawing should have a corresponding sequence identifier and that sequence identifier should be referenced with the sequence in the drawing or in the specification in the description of the drawing.

Appropriate sequence identifiers should be used to comply with sequence rules. The sequences in the specification should match the sequence listing and computer readable form (CRF) submitted with the application. Applicant is asked to review the specification for sequences that are not identified and correction is required. Applicant must provide a substitute computer readable form (CRF) copy of the "Sequence Listing", a substitute paper copy of the "Sequence Listing", an amendment of the specification to insert appropriate sequence identifiers, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code on page 8. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

It is noted that the cited occurrence of improper use is only exemplary and applicant should review the specification to correct any other use of embedded hyperlink and/or other form of browser-executable code.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 49-52 and 54-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to purified polypeptides that have the amino acid sequence of SEQ ID NO:2 or are degenerate variants of SEQ ID NO:2. Dependent claims are drawn to variants that are fragments comprising at least 5 amino acids and variants which are at least 60 or 80% identical to SEQ ID NO:2. The claims also include variants which have a serine at residue 26 and/or 44 and which do not have endopeptidase activity.

The specification discloses SEQ ID NO:2 as well as a variant where there is a serine at positions 26 and/or 44. Said variant lacks endopeptidase activity. The specification, on pages 9-10, states that "a degenerate variant refers to those polypeptides having conservative amino acid substitutions as compared to the base sequence." The specification does not define "conservative amino acid substitutions" but rather provides several non-limiting examples of such. The On-line Medical dictionary (http://cancerweb.ncl.ac.uk/cgi-bin/omd?conservative+substitution, accessed 1/23/2009) defines "conservative substitution" as a "substitution of one amino acid with another with generally similar properties (size, hydrophobicity, etc), such that the overall

functioning is likely not to be seriously affected." As there is no function required for the protein, it appears that any substitution could therefore be considered a conservative substitution and it does not appear that there is any limit on the number of substitutions that can be made to SEQ ID NO:2. Thus, there is no correlation between the structure of the variants and their function. Therefore, the specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that

"applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO:2 and a variant of SEQ ID NO:2 where there is a serine at position 26 and/or 44, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid and/or protein itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2datl966.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie *et al.* (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex (column 1, page 1306). As there is no function given for the claimed protein, there is not way to determine whether a given substitution is a conservative substitution and the claim therefore encompasses all substitutions, with no limit. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus because the genus is highly variant and very large. Therefore, applicant was not in possession of the claimed genus.

With regard to claim 50, the claim encompasses fragments that are at least 5 consecutive amino acids long and which are "immunologically reactive" with an anti-GBS phage lysin antibody. Presumably, "immunologically reactive with an anti-GBS phage lysin" means that the fragment is capable of binding to an anti-GBS phage lysin. However, epitopes consist of six amino acids (see Cruse *et al.*, Illustrated Dictionary of Immunol., 2nd ed., 2003, page 382). Therefore, applicant has not described any fragments that are 5 consecutive amino acids long that are immunologically reactive with an anti-GBS phage lysin.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 49-50 and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 49 is rendered vague and indefinite by the phrase "degenerate variant of SEQ ID NO:2." The specification, on pages 9-10, states that "a degenerate variant refers to those polypeptides having conservative amino acid substitutions as compared to the base sequence."

The specification does not define "conservative amino acid substitutions" but rather provides several non-limiting examples of such. The On-line Medical dictionary (http://cancerweb.ncl.ac.uk/cgi-bin/omd?conservative+substitution, accessed 1/23/2009) defines "conservative substitution" as a "substitution of one amino acid with another with generally similar properties (size, hydrophobicity, etc), such that the overall functioning is likely not to be seriously affected." In an article discussing conservative substitution, French *et al.* (J. Mol. Evol., 19:171-175, 1983) states that the degree of hydrophobicity of a residue, the conformational preferences of its backbone, and it's bulk are continuous properties and the extent to which a substitution is conservative is a matter of degree. Based on the definition of "conservative substitution" found in the art and the lack of a definition in the specification, it is not clear what changes can be made to SEQ ID NO:2 for the resulting protein to be a "degenerate variant." In fact, claims 54-55 make it clear that "conservative substitutions" such as serine for cysteine at positions 26 or 44, can lead to changes in function. Therefore, it is not clear what degree of similarity is sufficient or what function must be maintained for a given substitution to be a conservative substitution.

Claims 50 and 53 are broader than their parent claim. Fragments are not encompassed by a polypeptide which comprises SEQ ID NO:2 or a degenerate variant of SEQ ID NO:2.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 49-52 are rejected under 35 U.S.C. 102(a) as being anticipated by Telford *et al.* (WO02/34771, May, 2002; IDS filed 2/6/2004).

The instant claims are drawn to purified polypeptides with the amino acid sequence of SEQ ID NO:2 or degenerate variants of SEQ ID NO:2.

Telford *et al.* disclose a purified protein (as well as fragments of said protein which are at least 7 amino acids long) with the sequence of SEQ ID NO:1388 (see page 2, lines 1-5 and 25-

30, and page 140 of the sequence listing). SEQ ID NO:1388 is 92.7% identical to the instantly claimed SEQ ID NO:2. As there is no defined function for the protein, any substitution can be considered a conservative substitution, as it would not alter the function of the protein. Therefore, the protein disclosed by Telford *et al.* is considered a degenerate variant.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571)272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian J Gangle/
Examiner, Art Unit 1645

/Mark Navarro/
Primary Examiner, Art Unit 1645